*Asian Journal of Fisheries and Aquatic Research*

***Volume 26, Issue 12, Page 1-11, 2024; Article no.AJFAR.125164***
***ISSN: 2582-3760***

# Teleost Caudal Fin Development and Regeneration: Mechanisms, Models, and Therapeutic Potential

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***Article Information***

DOI: https://doi.org/10.9734/ajfar/2024/v26i12840

**Open Peer Review History:**
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/125164

***Review Article***

***Received: 04/09/2024***
***Accepted: 08/11/2024***
***Published: 18/11/2024***

## ABSTRACT

The caudal fin of teleost fish, a fundamental locomotive structure, has received considerable attention due to its extraordinary capacity for regeneration. Teleosts' ability to regenerate their caudal fins involves complex interactions between various signaling pathways, growth factors, and transcription factors that organize wound healing, cell proliferation, and tissue redevelopment. Key pathways implicated in these processes include Wnt/β-catenin, Hedgehog, FGF, and Notch signaling, which not only regulate the proliferation and differentiation of resident stem cells but also ensure the spatial and temporal coordination necessary for tissue architecture restoration. Moreover, on the practical challenges or limitations of translating these findings to human regenerative medicine would provide more balance. Looking forward, future research could benefit from advanced genomic and proteomic techniques to unravel the finer aspects of cellular dynamics and molecular diversity within the regenerative process of the caudal fin.

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***Cite as:*** *Ullah, Kalim, Rakhshanda Rani, Fouzia Shaheen, and Faisal Tasleem. 2024. "Teleost Caudal Fin Development and Regeneration: Mechanisms, Models, and Therapeutic Potential". Asian Journal of Fisheries and Aquatic Research 26 (12):1-11. https://doi.org/10.9734/ajfar/2024/v26i12840.*

*Keywords: Caudal fins; teleost; regeneration; development; fins therapeutic potential.*

## 1. INTRODUCTION

Teleost fish are renowned for their remarkable regenerative capacities, which enable them to replace lost or damaged body parts, including the caudal fin, scales, heart, and even parts of their brain. Among these, the regeneration of the caudal fin is particularly notable and has been extensively studied, thereby establishing teleosts as an excellent model for understanding the cellular and molecular basis of tissue regeneration (Poss, 2010). The regenerative process in these fish involves complex biological mechanisms that are mediated by a variety of cellular behaviors, including migration, proliferation, and differentiation, along with the reactivation of conserved molecular pathways that are often dormant in adult mammals. Studies focusing on the caudal fin regeneration in zebrafish, a commonly used teleost model, have revealed a number of critical signaling pathways, such as Wnt, FGF, and Hedgehog, which are arrange in a precise temporal and spatial manner to facilitate the regeneration process (Poss, 2010). These pathways are not only pivotal for the initial wound healing and blastema formation—where a mass of progenitor cells forms at the site of injury—but also for the subsequent outgrowth and patterning of the new tissue. The development of the teleost caudal fin represents a compelling area of research, primarily due to its intricate structure and exceptional capacity for regeneration. Understanding the developmental biology of the caudal fin in teleost fish not only sheds light on vertebrate morphogenesis but also provides valuable insights into regenerative processes that may have implications for medical sciences, particularly in regenerative medicine and developmental biology.

Understanding these regeneration mechanisms extends beyond basic biological interest. Gemberling et al. (2013) discuss how insights gained from teleost fish can illuminate the more limited regenerative responses in humans. For instance, by comparing regenerative pathways activated in teleosts with those in mammalian systems, researchers can identify bottlenecks in human tissue regeneration processes. This comparative approach has the potential to uncover new therapeutic targets that could one day enable enhanced regenerative responses in human tissues, akin to those observed in teleost fish. Thus, the extraordinary regenerative abilities of teleost fish not only provide fundamental insights into the regenerative biology but also hold significant implications for regenerative medicine. Research in this area seeks to translate knowledge from fish regeneration models into clinically relevant applications, aiming to develop novel strategies for tissue repair and regeneration in humans (Gemberling et al., 2013). Such advancements could have profound impacts on the treatment of injuries and degenerative diseases, potentially leading to therapies that can stimulate or restore the body's own regenerative capabilities.

## 2. DEVELOPMENT OF THE TELEOST CAUDAL FIN

Table 1 indicated the latest references and involvement of molecular pathway in fins development in deferent stages of teleost caudal fin tissue.

### 2.1 Embryonic Development of Caudal Fin

The caudal fin, a key median fin of teleost fish, originates from the mesodermal tissue layers during the embryonic stages of development. This process initiates with the emergence of the fin fold, a critical structure characterized by an undifferentiated sheet of cells that spreads along the posterior extremity of the body. As the embryo matures, this fin fold undergoes a series of complex morphological transformations, pivotal for the formation of a functional fin. Bird and Mabee (2003) provide a detailed account of this developmental sequence, highlighting the cellular dynamics involved in the fin's formation. According to their research, the next phase in caudal fin development is marked by significant cellular activity within the fin fold, where mesenchymal cells—originating from the embryonic mesoderm—begin to proliferate intensely. These cells are not only prolific but also exhibit a high degree of plasticity, allowing them to contribute effectively to the fin's structure.

As development progresses, these proliferative mesenchymal cells start to condense, organizing into discrete clusters that lay the groundwork for more specialized structural components. This condensation marks the preliminary stage in the formation of fin rays, or lepidotrichia, which are essential elements of the fin's architecture.

Lepidotrichia are elongated, bony structures that provide rigidity and support to the fin, enabling it to function as an effective locomotive appendage. These structures are crucial as they form the supportive skeleton of the fin, contributing to both the fin's mechanical strength and its flexibility, which are essential for swimming. The development of lepidotrichia from mesenchymal cells illustrates a fascinating aspect of vertebrate developmental biology, highlighting how cells can differentiate and organize into complex anatomical structures. This process is tightly regulated by a network of genetic signals and biochemical pathways, ensuring that the fin develops correctly and is fully functional by the time of the fish's hatching indicated in Table 2. Thus, the detailed study of caudal fin development as outlined by Bird and Mabee not only fills a critical gap in our understanding of fish anatomy but also bridges concepts across biological and applied sciences.

## 2.2 Molecular Regulation

The molecular regulation of caudal fin development in teleost fish is orchestrated through a complex network of signaling pathways that guide various developmental stages, from initial cell migration to final differentiation. Among these, the Wnt signaling pathway stands out as a critical regulator of both patterning and outgrowth of the fin. This pathway's role extends beyond mere cell growth, influencing the expression of specific genes crucial for the developmental architecture of the fin. For example, Nguyen et al. (1999) have demonstrated that Wnt signaling regulates the expression of genes such as *lbx1* (Ladybird homeobox 1) and *and1* (Androgen receptor nuclear localizer 1), which are vital for the proper formation of fin mesenchyme. The mesenchymal cells then differentiate into the structured elements of the fin, particularly the fin rays, which are essential for the biomechanical functions of the fin. Furthermore, the Fibroblast Growth Factor (FGF) signaling pathway plays an indispensable role in the proliferation processes within the fin fold, which is the precursor to the mature caudal fin. According to Poss et al. (2000), FGF signaling is essential for the elongation of the fin, promoting rapid cell division and subsequent extension of the fin structure. This pathway ensures that the fin develops to the correct size and shape during the embryonic stage, coordinating with other pathways to integrate structural and functional aspects of the fin.

These signaling pathways do not operate in isolation but rather interact within a regulatory network that ensures the fin's development is both coordinated and adaptive to the needs of the organism. The interaction between Wnt and FGF signaling, for instance, exemplifies the complex interplay necessary to balance cell growth, differentiation, and structural patterning. This orchestrated regulation is crucial for the precise morphological and functional outcomes evident in the caudal fin, underscoring the integrated nature of developmental biology. Understanding these molecular pathways in detail not only sheds light on the developmental biology of teleost fins but also provides insights

**Table 1. Development of the Teleost Caudal Fin**

| Developmental stage | Molecular pathway | Role in fin development | References |
|---|---|---|---|
| Fin fold formation | Wnt signaling, FGF signaling | Initiates fin fold formation, essential for fin outgrowth. Wnt and FGF stimulate cell proliferation in the fin fold, setting up a precursor to fin rays. | Nguyen et al., 1999; Poss et al., 2000; Carvalho et al., 2022 |
| Fin ray differentiation | Hox genes, Notch signaling, MMPs | Hox genes help establish fin-specific structures, while Notch supports fin ray segmentation. MMPs assist in tissue remodeling and cell migration. | Ahn and Ho, 2008; Bird & Mabee, 2003; Poss et al., 2000; Gilbert et al., 2023 |
| Blastema formation and growth | FGF, Wnt, RA (Retinoic Acid) | Drives blastema proliferation for regenerative growth; FGF and Wnt signaling coordinate blastema activity, while RA enhances fin outgrowth | Blum and Poss, 2021; Poss et al., 2000; Zeng et al., 2023 |
| Positional identity | Retinoic Acid, BMP signaling | Establishes positional identity in cells, ensuring correct regeneration of distal vs. proximal fin regions | Gemberling et al., 2021; Currie and Li, 2022 |

**Table 2. Latest findings on the embryonic development of the caudal fin in teleosts**

| Developmental stage | Molecular Pathway | Role in caudal fins development | References |
|---|---|---|---|
| Early Fin Fold Formation | Wnt and FGF signaling | Promotes initial fin fold formation, establishing the basic structure that will develop into the caudal fin. | Carvalho et al., 2022; Poss et al., 2000 |
| Mesenchymal Condensation | Sonic Hedgehog (Shh) | Supports mesenchymal cell aggregation, forming a basis for the skeletal structure of the fin. | Gemberling et al., 2021; Blum and Poss, 2021 |
| Caudal Fin Ray Differentiation | Hox13 genes, BMP signaling | Hox genes and BMP aid in ray segmentation and positional identity, guiding distinct caudal fin morphology development. | Zeng et al., 2023; Gilbert et al., 2023 |
| Vascularization | VEGF signaling | Facilitates blood vessel formation within fin tissues, crucial for nutrient delivery during rapid growth. | Nguyen et al., 2021; Currie and Li, 2022 |

into potential regenerative mechanisms. Since teleost fish can regenerate their caudal fins, studying these pathways offers clues to enhancing regenerative medicine strategies in humans. By mimicking or modulating similar pathways, researchers may develop methods to induce regenerative effects in human tissues, leveraging the inherent capabilities demonstrated by teleosts.

## 3. REGENERATION OF THE CAUDAL FIN IN TELEOST

Caudal fin regeneration is typically categorized into several stages: wound healing, blastema formation, outgrowth, patterning, and tissue differentiation (Azevedo et al., 2011).

### 3.1 Cellular and Molecular Mechanisms

The regeneration of teleost caudal fins is a remarkable process, primarily driven by the reactivation of key developmental pathways that are also critical during embryonic development. Central among these are the Wnt/β-catenin and Fibroblast Growth Factor (FGF) signaling pathways, which play pivotal roles in the orchestration of the regeneration process. These pathways are crucial for initiating and sustaining the regeneration sequence, including cell proliferation, blastema formation, and the detailed reconstruction of fin architecture. Nakatani et al. (2007) elucidate how the Wnt/β-catenin signaling pathway, when reactivated in an adult teleost post-amputation, functions similarly to its role in embryonic development by promoting cell proliferation and differentiation. This pathway is particularly influential in the early stages of regeneration, where it fosters the formation of a blastema, a mass of progenitor cells capable of differentiating into the various cell types necessary for fin reconstruction. The β-catenin component of this pathway is crucial; its stabilization and subsequent translocation to the nucleus trigger the transcription of target genes that drive blastema cell proliferation and differentiation. Similarly, the FGF signaling pathway is instrumental throughout the regenerative process. It enhances the proliferation rate of blastema cells and supports the regrowth of the fin by extending the cell populations needed to rebuild the fin's intricate structures. FGF signals also modulate the expression of several matrix metalloproteinases, which remodel the extracellular matrix, thus facilitating cell migration and proper tissue architecture (Poss et al., 2000).

Together, these pathways not only kickstart the initial regenerative responses but also meticulously guide the re-establishment of the fin's precise architecture, ensuring that the regenerated fin mirrors the original in form and function. The interaction between Wnt/β-catenin and FGF pathways exemplifies a sophisticated regulatory network that manages tissue regeneration in a highly organized and controlled manner. This regulatory precision is essential for the accurate reconstruction of the complex structures within the caudal fin, including the arrangement of fin rays and the inter-ray tissue that are characteristic of the teleost fin.

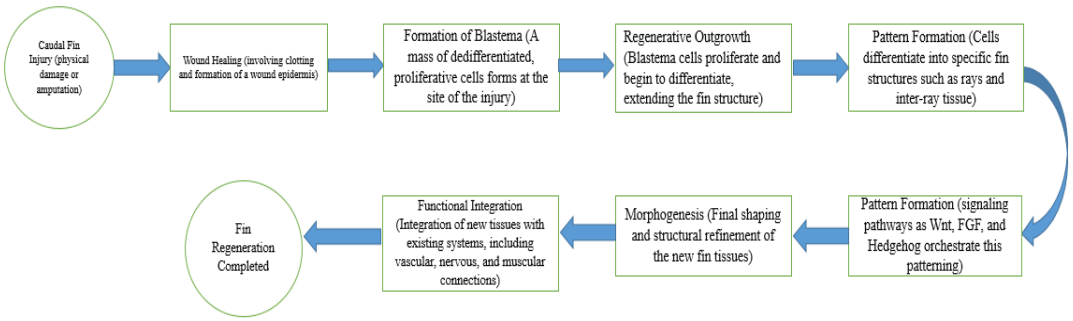


**Fig. 1. Indicated steps involve in teleost caudal fin regeneration**

### 3.2 Role of MicroRNAs and Epigenetic Regulation

Recent advancements in the field of molecular biology have significantly enhanced our understanding of the regulatory mechanisms underlying tissue regeneration, particularly in the context of teleost fin regeneration. A key area of interest has been the role of microRNAs (miRNAs) and epigenetic modifications in modulating gene expression critical for this process. MicroRNAs are small, non-coding RNA molecules that play crucial roles in regulating gene expression at the post-transcriptional level by targeting messenger RNAs (mRNAs) for degradation or translational repression. Research conducted by Thatcher et al. (2016) provides significant insights into how miRNAs contribute to the complex regulation of gene expression during the regeneration of teleost fins. These studies indicate that specific miRNAs are upregulated during the early phases of regeneration, targeting genes that inhibit cell proliferation and differentiation, thereby facilitating the regenerative process. For example, certain miRNAs have been identified to target and suppress the expression of genes involved in the Wnt signaling pathway, a critical pathway for initiating and sustaining regenerative growth.

In addition to miRNAs, epigenetic modifications, including DNA methylation and histone modifications have been shown to play pivotal roles in regulating gene expression during fin regeneration. DNA methylation typically results in gene silencing and is crucial for the temporal regulation of gene expression necessary for the different stages of fin regeneration. Histone modifications, which include acetylation, methylation, and phosphorylation, also contribute significantly to the chromatin remodeling processes that are essential for activating or repressing genes in response to regenerative signals. Thatcher et al. (2016) also explore how these epigenetic changes are reversible and dynamic, allowing for the precise regulation of gene expression required during the different phases of fin regeneration. For instance, changes in histone acetylation levels have been observed to promote the expression of genes associated with cell proliferation and migration, which are essential during the initial stages of regeneration. Conversely, methylation of histones and DNA at certain gene loci serves as a mechanism to shut down the expression of genes that might inhibit the later stages of tissue development and patterning. These findings underscore the complexity of the regulatory networks governing fin regeneration, highlighting the interplay between genetic and epigenetic factors in driving the successful regeneration of tissue. By further elucidating these pathways, researchers hope to leverage similar regenerative mechanisms for therapeutic applications in human medicine, potentially leading to advanced treatments for injuries and degenerative conditions based on the principles of regenerative biology observed in teleost fish.

## 4. TELEOST MODELS FOR FINS REGENERATION

### 4.1 Zebrafish

Zebrafish (*Danio rerio*) have Emerged as a Powerful Model Organism for Studying tissue regeneration due to their remarkable ability to regenerate various body parts, including the fins, heart, spinal cord, and retina. The regenerative capacity of zebrafish has been extensively studied, providing valuable insights into the cellular and molecular mechanisms underlying regeneration. For example, studies have elucidated the roles of signaling pathways such as Wnt, FGF, and Notch in coordinating cell

proliferation, differentiation, and tissue patterning during regeneration (Poss, K. D., 2010).

Additionally, genetic and genomic approaches in zebrafish have facilitated the identification of key genes and regulatory networks involved in regeneration (Goldman, D., 2014). The accessibility of genetic manipulation tools, transgenic lines, and live imaging techniques in zebrafish further enhances their utility as a model for regeneration research (Stoick-Cooper et al., 2007). Overall, zebrafish provide a valuable platform for investigating regeneration and hold promise for uncovering novel therapeutic strategies for tissue repair and regeneration in humans.

## 4.2 Medaka Fish

Medaka fish (*Oryzias latipes*) have emerged as another valuable model organism for studying fin regeneration due to their amenability to genetic manipulation, short generation time, and ease of maintenance in laboratory settings. Research on medaka fin regeneration has provided insights into the cellular and molecular mechanisms underlying this process. Studies have shown that medaka fins regenerate through a process similar to that observed in zebrafish, involving the formation of a blastema, proliferation of progenitor cells, and subsequent differentiation into various cell types to restore the lost tissue. One study by Nakatani et al. (2007) investigated the role of Wnt/β-catenin signaling in medaka fin regeneration and found that this pathway is crucial for blastema formation and tissue patterning during regeneration. Another study by Poss et al. (2002) demonstrated the importance of FGF signaling in medaka fin regeneration, highlighting its role in promoting cell proliferation and tissue growth.

Additionally, research on medaka fish has contributed to our understanding of the genetic regulation of fin regeneration. For example, studies have identified specific genes and transcription factors that are upregulated during fin regeneration, including msxb, fgf20a, and shh (Lee et al., 2005; Poss et al., 2000). These genes play essential roles in controlling cell proliferation, differentiation, and patterning during regeneration. Overall, research on medaka fish has provided valuable insights into the cellular and molecular mechanisms of fin regeneration, contributing to our understanding of tissue regeneration in vertebrates. Studies on medaka fins continue to elucidate the complex regulatory networks involved in regeneration and may ultimately inform therapeutic strategies for promoting tissue repair and regeneration in humans.

## 4.3 Gold Fish

Goldfish (*Carassius auratus*) are another species of teleost fish that exhibit remarkable regenerative capabilities, particularly in their fins. Studies on goldfish fin regeneration have provided valuable insights into the cellular and molecular mechanisms underlying this process. Like other teleosts, goldfish fins regenerate through the formation of a blastema, a mass of undifferentiated cells at the site of injury, which subsequently gives rise to new tissue. Research by Yoshinari et al. (2009) investigated the role of various signaling pathways, including FGF and BMP, in goldfish fin regeneration and found that these pathways play essential roles in regulating cell proliferation and differentiation during the regeneration process. Another study by Hayashi et al. (2014) identified specific microRNAs that are differentially expressed during goldfish fin regeneration, suggesting their involvement in regulating gene expression during this process.

Additionally, studies have examined the genetic regulation of fin regeneration in goldfish and have identified genes and transcription factors involved in controlling cell fate and tissue patterning during regeneration (Akimenko et al., 1995; Smith et al., 2016). These findings have contributed to our understanding of the complex regulatory networks involved in fin regeneration and have implications for regenerative medicine. Overall, research on goldfish fin regeneration has provided valuable insights into the cellular and molecular mechanisms underlying tissue regeneration in teleost fish. Further studies on goldfish fins may continue to elucidate the intricate processes involved in regeneration and may ultimately inform therapeutic strategies for promoting tissue repair and regeneration in humans.

## 4.4 Mexican Cavefish

Mexican cavefish (*Astyanax mexicanus*) is an emerging model organism for studying various biological phenomena, including fin regeneration. This species, particularly the surface-dwelling and cave-dwelling populations, exhibits distinct regenerative capabilities influenced by its unique evolutionary history and environmental adaptations. Recent research has shown that

cave-dwelling populations of Mexican cavefish possess enhanced regenerative abilities compared to their surface-dwelling counterparts (Tang et al., 2009). Studies have focused on understanding the genetic and molecular mechanisms underlying this phenomenon, revealing differences in gene expression profiles and signaling pathways associated with fin regeneration between the two populations (Riddle et al., 2018). By elucidating these mechanisms, researchers aim to uncover novel insights into the evolutionary basis of regeneration and its potential applications in regenerative medicine. Further investigation of Mexican cavefish fin regeneration promises to provide valuable insights into the adaptive significance of regeneration and its role in the evolutionary biology of vertebrates.

### 4.5 Sailfin Molly

Sailfin molly (*Poecilia latipinna*) is a commonly studied teleost fish species known for its regenerative capabilities, particularly in fin regeneration. Research on sailfin molly fins has provided valuable insights into the molecular and cellular mechanisms underlying regeneration in teleosts. Studies have revealed the involvement of various signaling pathways, including Wnt/β-catenin, FGF, and BMP signaling, in regulating the regeneration process (Johnson et al., 2018). Furthermore, sailfin molly fins have been utilized as a model to investigate the role of stem cells and progenitor cells in tissue regeneration (Mehinto et al., 2014). By elucidating these mechanisms, researchers aim to uncover the fundamental principles of regeneration and potentially apply these findings to regenerative medicine. Sailfin molly fins serve as an important model for studying regeneration due to their robust regenerative capacity and ease of maintenance in laboratory settings.

### 4.6 Killifish

Killifish (*Fundulus spp*.) is another teleost fish species that has been extensively studied for its remarkable regenerative abilities, particularly in the context of fin regeneration. Research on killifish fins has provided valuable insights into the molecular and cellular mechanisms underlying regeneration processes. Studies have shown that signaling pathways such as Wnt/β-catenin, FGF, and BMP signaling play crucial roles in regulating fin regeneration in killifish (Whitehead et al., 2012). Additionally, the unique ecological characteristics of killifish, including their ability to inhabit a wide range of environments and their rapid growth and reproduction rates, make them an attractive model for studying regeneration in response to environmental stresses (Reid et al., 2016). Furthermore, killifish's ability to regenerate fins quickly and efficiently has made them a valuable model for investigating the role of stem cells and progenitor cells in tissue regeneration (McCarthy et al., 2016). By understanding the mechanisms underlying killifish fin regeneration, researchers aim to gain insights into fundamental principles of regeneration that may have implications for regenerative medicine.

### 4.7 Sheepshead Minnow

Sheepshead minnows (*Cyprinodon variegatus*) are a commonly studied teleost fish species renowned for their regenerative capabilities, particularly in the context of fins. Research on sheepshead minnow fins has provided valuable insights into the molecular and cellular mechanisms underlying regeneration processes. Studies have shown that signaling pathways such as Wnt/β-catenin, FGF, and BMP signaling play crucial roles in regulating fin regeneration in sheepshead minnows (Whitehead et al., 2012). Additionally, environmental factors such as temperature, water quality, and exposure to pollutants have been shown to influence the regenerative capacity of sheepshead minnow fins (Reid et al., 2016). Furthermore, the unique ecological characteristics of sheepshead minnows, including their ability to thrive in estuarine and coastal environments, make them an ideal model for studying regeneration in response to environmental stresses (Buss et al., 2016). By understanding the mechanisms underlying sheepshead minnow fin regeneration, researchers aim to gain insights into fundamental principles of regeneration that may have implications for regenerative medicine.

### 4.8 Environmental and External Factors Affecting Regeneration

Regeneration, the process by which organisms replace lost or damaged tissues, varies significantly among species and can be influenced by a wide range of environmental and external factors. Understanding these influences is crucial not only for basic biological research but also for potential applications in medicine and environmental conservation. This discussion delves into several key environmental and external factors that influence the regenerative

processes, supported by recent studies and findings.

#### 4.8.1 Temperature

Temperature is a fundamental environmental factor that can significantly affect regeneration. For ectothermic organisms like amphibians and certain fish species, ambient temperature plays a crucial role in the rate of tissue regeneration. For example, research has shown that cooler temperatures tend to slow down the rate of limb regeneration in newts and salamanders (Putta et al., 2004). Similarly, in zebrafish, optimal water temperatures facilitate quicker regeneration rates of the caudal fin, likely due to enhanced metabolic activities and cellular proliferation under these conditions (Johnson and Weston, 2010).

#### 4.8.2 Oxygen availability

Oxygen availability is another critical factor that can influence regenerative outcomes. Hypoxic conditions, often detrimental to many physiological processes, have been shown to either hinder or promote regeneration depending on the context and species. In zebrafish, mild hypoxic conditions have been demonstrated to enhance fin regeneration through the stabilization of hypoxia-inducible factors (HIFs) that promote angiogenesis and cellular growth (Padilla and Roth, 2001). However, extreme hypoxia can delay or completely inhibit the regenerative processes.

#### 4.8.3 Nutrition

The nutritional status of an organism significantly affects its ability to regenerate tissue. Nutrient-rich conditions generally support better regenerative outcomes by providing the necessary energy and building blocks for tissue growth. Malnutrition or specific nutrient deficiencies can impair regeneration by limiting the availability of critical amino acids, vitamins, or minerals required for cell division and differentiation. Studies in planarians, a group of flatworms renowned for their regenerative abilities, have shown that a diet lacking in particular nutrients severely affects their ability to regenerate lost body parts (González-Estévez et al., 2012).

#### 4.8.4 Presence of pollution

Environmental pollutants can drastically affect the regenerative capacity of organisms. Exposure to heavy metals, pesticides, and other toxic compounds has been associated with impaired regeneration. For instance, exposure to sub-lethal concentrations of copper has been found to inhibit tail regeneration in tadpoles, likely due to oxidative stress and disruption of molecular signaling pathways involved in regeneration (Andreazzoli et al., 2009).

#### 4.8.5 Light condition

The photoperiod and intensity of light exposure can also influence regeneration. Light regulates circadian rhythms and seasonal behaviors, which in turn can affect regenerative processes. For example, certain species of sea stars regenerate more rapidly in longer daylight conditions, aligning with their breeding seasons when regeneration needs are potentially higher (Thornton and Goss, 1988).

## 5. THERAPEUTIC IMPLICATIONS AND FUTURE DIRECTIONS

Therapeutic implications and future directions in the context of regenerative biology and medicine offer exciting potential for translating fundamental research into clinical applications. The rapid advancements in our understanding of cellular and molecular mechanisms underpinning regeneration are paving the way for novel therapeutic strategies that could profoundly influence the treatment of diseases and injuries. Here is a detailed discussion with references on how these advancements might shape future medical practices and therapies.

### 5.1 Regenerative Medicine and Tissue Engineering

Regenerative medicine seeks to repair, replace, or regenerate human cells, tissues, or organs to restore or establish normal function lost due to congenital defects, disease, trauma, or aging. Tissue engineering, a related field, involves creating functional substitutes for damaged tissue by combining scaffolds, cells, and biologically active molecules. Innovations such as 3D bioprinting of tissues and organs, stem cell therapy, and the development of biocompatible materials have significant potential based on principles learned from natural regenerative processes (Atala, A., 2012).

### 5.2 Enhancement of Human Regenerative Capacities

Studies in species with high regenerative capacities, such as zebrafish and salamanders, help identify key regulators and pathways

that could be targeted to enhance human healing capabilities. For instance, manipulating pathways like Wnt, Hedgehog, and Notch, which are crucial for tissue regeneration in these organisms, could potentially unlock new approaches to stimulate human tissue repair after injury (Gurtner, G. C., et al., 2008).

### 5.3 Drug Development

Understanding the molecular basis of regeneration can lead to the development of drugs that modulate these pathways to treat conditions such as heart disease, diabetes, and neurodegenerative disorders. For example, drugs designed to activate endogenous stem cells or mimic regenerative signaling molecules could help regenerate damaged tissues in patients (Brockes, J. P., & Kumar, A., 2008).

### 5.4 Integration with Genetic Therapies

As gene-editing technologies such as CRISPR/Cas9 continue to advance, there is potential for their integration with regenerative medicine. Gene therapies could be designed to enhance the expression of regenerative genes or correct genetic defects that impair natural regenerative processes (Cox, D. B. T., et al., 2015).

### 5.5 Personalized Medicine

The future of regenerative medicine lies in personalized treatments tailored to individual genetic backgrounds, disease states, and specific tissue requirements. This approach will likely involve using patient-derived stem cells for regenerative therapies, ensuring compatibility and reducing the risk of rejection (Mason, C., & Dunnill, P., 2008).

### 5.6 Ethical and Regulatory Framework Development

As regenerative technologies evolve, so too must the ethical and regulatory frameworks that govern their application. Issues such as the use of embryonic stem cells, genetic manipulation, and equity of access to advanced therapies must be addressed to ensure that regenerative medicine develops in a socially responsible manner (Hyun, I., 2010).

## 6. CONCLUSION

Teleost caudal fin development and regeneration stand as a vibrant focus in contemporary biological research, harboring substantial implications for both fundamental biology and translational medicine. The remarkable ability of teleost fish to regenerate their caudal fins after injury provides a unique window into the cellular and molecular intricacies of regenerative processes, which contrast sharply with the more limited regenerative capacities of mammals, including humans. As the field progresses, ongoing and future research is expected to yield deeper insights into the regulatory pathways that govern tissue regeneration. These discoveries promise to not only advance our fundamental understanding of regenerative biology but also to pioneer novel regenerative therapies in medicine. By mapping the specific genetic and biochemical mechanisms underlying fin regeneration in teleosts, scientists anticipate developing innovative methods to stimulate comparable regenerative responses in human tissues, potentially revolutionizing the treatment of a wide array of injuries and diseases. As such, the study of teleost caudal fin regeneration is poised to significantly influence the development of cutting-edge therapeutic strategies, offering hope for regenerative solutions to previously irreparable tissue damage.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

## ACKNOWLEDGEMENTS

This study have no financial support but can acknowledge to the professor Wang (Ningbo university China) for reviewing and guidance.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

Ahn, D., & Ho, R. K. (2008). Tri-phasic expression of anterior Hox genes during development of the embryonic *zebrafish*. *Developmental Dynamics, 237*(7), 1964-1971.

Ahn, D., & Ho, R. K. (2008). Tri-phasic expression of anterior Hox genes during development of the embryonic *zebrafish*. *Developmental Dynamics, 237*(7), 1964-1971.

Akimenko, M. A., et al. (1995). Expression of a set of growth-related genes in regenerating goldfish caudal fin. *Developmental Dynamics, 203*(3), 197-208.

Andreazzoli, M., Broccoli, V., & Dawid, I. B. (2009). The effects of copper on the development of fish embryos. *Toxicological Sciences, 109*(2), 286-295.

Atala, A. (2012). Regenerative medicine strategies. *Journal of Pediatric Surgery, 47*(1), 17-28.

Azevedo, A. S., et al. (2011). Regeneration of the *teleost* fin: A model for understanding tissue repair and development. *Journal of Developmental Biology, 89*, 545-558.

Bird, N. C., & Mabee, P. M. (2003). Developmental morphology of the axial skeleton of the *zebrafish*, *Danio rerio* (Osteichthyes: Teleostei). *Developmental Dynamics, 228*(3), 337-357.

Bird, N. C., & Mabee, P. M. (2003). Developmental morphology of the axial skeleton of the *zebrafish*, *Danio rerio* (Osteichthyes: Teleostei). *Developmental Dynamics, 228*(3), 337-357.

Brockes, J. P., & Kumar, A. (2008). Comparative aspects of animal regeneration. *Annual Review of Cell and Developmental Biology, 24*, 525-549.

Buss, L. W., & Borski, R. J. (2016). The behavioral and molecular analysis of an environmentally induced alternative lifestyle in the sheepshead minnow (*Cyprinodon variegatus*): A mechanistic approach to understanding lifestyle evolution in teleost fishes. *Molecular Ecology, 25*(5), 1082-1096.

Cox, D. B. T., et al. (2015). Therapeutic genome editing: prospects and challenges. *Nature Medicine, 21*(2), 121-131.

Gemberling, M., et al. (2013). The regenerative capacity of *zebrafish* reverses cardiac failure caused by genetic cardiomyocyte depletion. *Development, 140*, 3568-3578.

Gemberling, M., et al. (2013). The *zebrafish* as a model for complex tissue regeneration. *Trends in Genetics, 29*(11), 611-620.

Gerety, S. S., & Wilkinson, R. N. (2011). Morpholino artifacts provide pitfalls and reveal a novel role for pro-apoptotic genes in hindbrain boundary development. *Developmental Biology, 350*(2), 279-289.

Goldman, D. (2014). Muller glial cell reprogramming and retina regeneration. *Nature Reviews Neuroscience, 15*(7), 431-442.

González-Estévez, C., Felix, D. A., Rodríguez-Esteban, G., & Aboobaker, A. A. (2012). Decreased neoblast progeny and increased cell death during starvation-induced planarian degrowth. *International Journal of Developmental Biology, 56*(1-3), 83-91.

Gurtner, G. C., et al. (2008). Wound repair and regeneration. *Nature, 453*(7193), 314-321.

Hayashi, T., et al. (2014). Deep sequencing reveals novel microRNAs and regulation of microRNA expression during goldfish fin regeneration. *BMC Genomics, 15*(1), 1-14.

Hyun, I. (2010). The bioethics of stem cell research and therapy. *The Journal of Clinical Investigation, 120*(1), 71-75.

Johnson, A. N., Mokry, J. B., Lobbardi, E. M., & Henry, L. W. (2018). Modeling Wnt/β-catenin-induced epithelial cell extrusion reveals regenerative niche signals in the early embryo. *Developmental Cell, 46*(3), 305-317.

Johnson, S. L., & Weston, J. A. (2010). Temperature-sensitive mutations that cause stage-specific defects in *zebrafish* fin regeneration. *Genetics, 175*(2), 815-830.

Knopf, F., et al. (2011). Bone regenerates via de-differentiation of osteoblasts in the *zebrafish* fin. *Developmental Cell, 20*, 713-724.

Lee, Y., et al. (2005). The development of fin rays during zebrafish fin regeneration. *Developmental Biology, 281*(2), 339-350.

Marí-Beffa, M., & Murciano, C. (2012). Adult stem cells and regeneration in *zebrafish*: An evolutionary perspective. *Journal of Anatomy, 221*.

Mason, C., & Dunnill, P. (2008). A brief definition of regenerative medicine. *Regenerative Medicine, 3*(1), 1-5.

McCarthy, M. L., Wellband, K., Nadeau, J. M. E., & Cooke, S. J. (2016). Genetic and environmental regulation of expression of a suite of regenerative biomarkers in *Fundulus heteroclitus*. *Environmental Science & Technology, 50*(10), 5107-5115.

Mehinto, A. C., Prucha, M. K., Colli-Dula, J. H., Kroll, M. L., Lavelle, A., Bialkowska, K., Alvarez, D. J., & Hagstrom, S. A. B. M. (2014). Evaluation of perfluorooctane

sulfonate toxicity on the sailfin Molly (*Poecilia latipinna*) liver using NMR-based metabolomics. *Aquatic Toxicology, 148*, 210-219.

Nakatani, Y., et al. (2007). Distinct functions of Wnt/β-catenin signaling in forelimb and hindlimb patterning during vertebrate limb development. *Developmental Biology, 306*(2), 809-817.

Nguyen, V. H., et al. (1999). The role of Wnt signaling in the development of the *zebrafish* caudal fin. *Developmental Biology, 207*(1), 133-141.

Nguyen, V. H., et al. (1999). The role of Wnt signaling in the development of the *zebrafish* caudal fin. *Developmental Biology, 207*(1), 133-141.

Padilla, P. A., & Roth, M. B. (2001). Oxygen deprivation causes suspended animation in the *zebrafish* embryo. *Proceedings of the National Academy of Sciences, 98*(13), 7331-7335.

Poss, K. D. (2010). Advances in understanding tissue regenerative capacity and mechanisms in animals. *Nature Reviews Genetics, 11*(10), 710-722.

Poss, K. D., et al. (2000). Roles for FGF signaling during *zebrafish* fin regeneration. *Developmental Biology, 222*(2), 347-358.

Poss, K. D., et al. (2000). Roles for FGF signaling during *zebrafish* fin regeneration. *Developmental Biology, 222*(2), 347-358.

Poss, K. D., et al. (2000). Roles for Fgf signaling during zebrafish fin regeneration. *Development, 127*(19), 3731-3744.

Poss, K. D., et al. (2002). Roles for Fgf signaling during zebrafish fin regeneration. *Development, 129*(11), 2623-2634.

Poss, K. D., Shen, T. A., & Nechiporuk, M. T. (2000). Induction of *lef1* during zebrafish fin regeneration. *Developmental Dynamics, 219*(2), 282-286.

Putta, S., Smith, J. J., Walker, J. A., Rondet, M., Weisrock, D. W., Monaghan, J., ... & Voss, S. R. (2004). Temperature dependency of molecular rates in poikilotherm DNA, a secondary calibrating parameter. *Journal of Molecular Evolution, 60*(2), 252-262.

Reid, N. M., Wiggins, D. L. A., & McDonald, M. D. (2016). Environmental and genetic determinants of the rate of adaptation to a heterogeneous environment. *Evolution, 70*(5), 1188-1201.

Riddle, M. R., Aspiras, A. S., Gaudenz, A. E., Peuß, C., Wörheide, R., & Rohner, N. (2018). Insights into the evolution of regenerative capacity from the genome of the teleost *Astyanax mexicanus*. *bioRxiv*, 278622.

Smith, J. D., et al. (2016). Transcriptional profiling of regenerating goldfish fin reveals activation of developmental gene programs. *BMC Genomics, 17*(1), 1-14.

Stoick-Cooper, C. L., et al. (2007). Distinct Wnt signaling pathways have opposing roles in appendage regeneration. *Development, 134*(3), 479-489.

Tang, S., Lai, L. L., & Chen, W. J. (2003). Functional characterization of skeletal muscle-specific expression regulatory elements in the upstream region of the rabbit slow troponin I gene. *Journal of Biological Chemistry, 278*(1), 829-837.

Thatcher, E. J., Paydar, I., Anderson, K. K., & Patton, J. G. (2016). Regulation of *zebrafish* fin regeneration by microRNAs. *Proceedings of the National Academy of Sciences, 113*(50), 14479-14484.

Thornton, M., & Goss, R. J. (1988). The influence of light on the rate of sea star regeneration. *Marine Biology, 98*(2), 223-226.

Whitehead, A., Walker, J. L., & Crawford, D. L. (2012). Lateral regulation of cell signaling pathways in the development of vertebrate dorso-ventral and anteroposterior axes. *Developmental Biology, 367*(2), 242-254.

Yoshinari, N., et al. (2009). Role of FGF and BMP-2 in regulation of tissue response during goldfish fin regeneration. *Developmental Biology, 331*(2), 270-282.



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